IT IS CLAIMED:

1. A method of screening for molecules capable of binding to a selected test sequence in a duplex DNA, comprising

(i) constructing a duplex DNA test oligonucleotide having a screening sequence adjacent a selected test sequence, where a DNA binding protein is effective to bind to said screening sequence with a binding affinity that is substantially independent of such test sequence, but where DNA protein binding to the screening sequence is sensitive to binding of test molecules to such test sequence,

(ii) adding a test molecule to be screened to a test system composed of (a) said DNA binding protein, and (b) said duplex DNA test oligonucleotide having said screening and test sequences adjacent one another,

(iii) incubating the molecule in the test system for a period sufficient to permit binding of the molecule being tested to the test sequence in the duplex DNA, and

(iv) comparing the amount of binding protein bound to the duplex DNA before and after said adding.

2. The method of claim 1, where said test sequence is selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:600.

3. The method of claim 1, where the DNA screening sequence is from the HSV origin of replication and the binding protein is UL9.

4. The method of claim 3, wherein the DNA screening sequence is selected from the group consisting of SEQ ID NO:601, SEQ ID NO:602, and SEQ ID NO:615.

5. The method of claim 1, where the DNA screening sequence is the DNA-binding sequence of a restriction endonuclease and the binding protein is a restriction endonuclease.

6. The method of claim 1, where said comparing is accomplished using either a gel band-shift assay or a filter-binding assay.

7. A screening system for identifying molecules that are capable of binding to a test sequence in a target duplex DNA sequence, comprising

a duplex DNA having screening and test sequences adjacent one another,

a DNA binding protein that is effective to bind to said screening sequence in the duplex DNA with a binding affinity that is substantially independent of a test sequence adjacent the screening sequence, but which is sensitive to binding of molecules to such test sequence, and

means for detecting the amount of binding protein bound to the DNA.

8. The system of claim 7, where said test sequences are selected from the group of sequences consisting of SEQ ID NO:1 through SEQ ID NO:600.

9. The system of claim 7, where the DNA screening sequence is from the HSV origin of replication and the binding protein is UL9.

10. The system of claim 9, wherein the DNA screening sequence is selected from the group consisting of SEQ ID NO:601, SEQ ID NO:602, and SEQ ID NO:615.

11. The system of claim 7, where the DNA screening sequence is the DNA-binding sequence of a restriction endonuclease and the binding protein is a restriction endonuclease.

12. A method of identifying test sequences in duplex DNA to which binding of a test molecule is most preferred, comprising

(i) constructing a mixture of duplex DNA test oligonucleotides, where each oligonucleotide has (a) a screening sequence adjacent (b) a test sequence, where a DNA binding protein is effective to bind to said screening sequence with a binding affinity that is substantially independent of such test sequence, but where DNA protein binding to the screening sequence is sensitive to binding of test molecules to such test sequence, and (c) where test

oligonucleotides of the mixture contain different test sequences,

(ii) adding a test molecule to be screened to a test reaction composed of (a) said DNA binding protein, and (b) said duplex DNA test oligonucleotide mixture,

(iii) incubating the molecule in the test reaction for a period sufficient to permit binding of the molecule being tested to test sequences in the duplex DNA,

(iv) separating test oligonucleotides from test oligonucleotides bound to binding protein,

(v) amplifying the separated test oligonucleotides,

(vi) repeating steps (ii) to (v),

(vii) isolating the amplified test oligonucleotides,

(viii) sequencing the isolated test oligonucleotides.

13. The method of claim 12, where said test sequences are selected from the group of 256 possible four base sequences composed of A, G, C and T.

14. The method of claim 12, where said constructing includes selecting test sequences from the sequences presented as SEQ ID NO:1 to SEQ ID NO:600.

15. The method of claim 12, where in constructing the mixture of test oligonucleotides, said adjacent screening and test sequences are flanked by primer sequences.

16. The method of claim 15, wherein said amplifying is carried out by successively repeating the steps of (a) denaturing the duplex test oligonucleotides to produce single-strand fragments, (b) hybridizing the single strands with primers, complementary to the primer sequences in the oligonucleotides, to form strand/primer complexes, (c) generating double-strand fragments from the strand/primer complexes in the presence of DNA polymerase and all four deoxyribonucleotides, and (d) repeating steps (a) to (c) until a desired degree of amplification has been achieved.

17. The method of claim 16, where the amplification steps are repeated 1-8 times.

18. The method of claim 12, wherein said amplifying is carried out by cloning the separated test oligonucleotides into a vector, passaging vectors carrying the test oligonucleotides in appropriate host cells, culturing the host, isolating the vectors, and obtaining the test oligonucleotides from the vectors.

19. The method of claim 12, where said isolating is accomplished by cloning the amplified test oligonucleotides into a cloning vector.

20. The method of claim 12, where said separating is accomplished by passing the test reaction through a filter, where said filter is capable of capturing DNA:protein complexes but not DNA that is free of protein.

21. The method of claim 20, where said filter is a nitrocellulose filter.

22. The method of claim 12, where the DNA screening sequence is from the HSV origin of replication and the binding protein is UL9.

23. A method for altering the binding characteristics of a DNA-binding protein to a duplex DNA, comprising

identifying in the duplex DNA (i) a binding site for the DNA-binding protein, where said site comprises a series of contiguous paired nucleotides, and (ii) a target region adjacent the binding site,

selecting a small molecule characterized by sequence-preferential binding to the target region, where, when the small molecule is bound to the target region, the small molecule is adjacent to the site for the DNA-binding protein or overlapping the site for the DNA-binding protein by at least one nucleotide pair, and

contacting the duplex DNA with the small molecule at a concentration effective to alter binding of the DNA-binding protein to its binding site.

24. The method of claim 23, where contacting the duplex DNA with the small molecule inhibits the binding of the DNA-binding protein to its binding site.

25. The method of claim 23, where contacting the duplex DNA with the small molecule enhances the binding of the DNA-binding protein to its binding site.

26. The method of claim 23, where the DNA binding protein is a eucaryotic general transcription factor and the target region is selected from DNA sequences adjacent the binding site for the eucaryotic transcription factor.

27. The method of claim 26, where the transcription factor is TFIID.

28. The method of claim 27, where the region is selected from the group of DNA sequences consisting of SEQ ID NO:1 to SEQ ID NO:600.

29. The method of claim 23, where the DNA binding protein is a eucaryotic general transcription factor and the small molecule binds, in addition to the target region, 1 to three nucleotide pairs of the DNA-binding protein's binding site.

30. The method of claim 29, where the eucaryotic general transcription factor is TFIID, and the small molecule binds to (i) the target region, and (ii) up to two nucleotides of the binding site for the eucaryotic transcription factor, where the nucleotides are contiguous to the target region.

31. The method of claim 23, where the DNA binding protein is a DNA replication factor.

32. A method for inhibiting the binding of a DNA-binding protein to duplex DNA, comprising

contacting a compound with a duplex DNA which contains a test sequence adjacent a screening sequence, where the DNA binding protein is effective to bind to the screening sequence with a binding affinity that is substantially independent of said test sequence, further where the binding of said compound to the test sequence inhibits the binding of the protein to the screening sequence.

33. The method of claim 32, wherein the compound is identified by the steps of

preparing a series of duplex nucleic acid fragments, each containing a test sequence composed of one of the 4N possible permutations of sequences in a sequence of base pairs having N-basepairs, where said test sequence is adjacent the screening sequence,

measuring the binding affinity of the DNA binding protein to each of the series of nucleic acid fragments in the presence of the compound, and

selecting the compound if it lowers the binding affinity of the DNA binding protein for the screening sequence.